

REMARKS

The last Office Action of September 26, 2003 has been carefully considered. Reconsideration of the instant application in view of the foregoing amendments and the following remarks is respectfully requested.

Claims 20-43 are pending in the application. Claims 20-26, 28, 29, 31 and 38 have been amended. Claims 27 and 37 have been canceled. Claims 44-49 have been added. A total of 28 claims is now on file. The claim surcharge for the additional claims is enclosed.

It is noted that claims 20-37 are rejected under 35 U.S.C. §112, first paragraph, as the specification not enabling any person skilled in the art to which it pertains, or with which it is most clearly connected, to use the invention commensurate with the scope of the claims. Claims 20-43 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 stands rejected under 35 U.S.C. §102(b) as being anticipated by the references as cited from PTO form 1449. Hallas (reference Y of PTO 1449) (hereinafter: "Hallas"), Aaron et. Al. (reference X of PTO 1449) (hereinafter: "Aaron"), Aaron et. al [R] (J. Chem. Soc. (1963) pp 2655-2662) (hereinafter: "Aaron II"), Barker et al (J. Chem. Soc. section B: Physical Organic) (1969), vol. 9 pp 1068-1071 (hereinafter: "Barker") or U.S. Patent No. 4,320,940 (hereinafter: "Mueller").

Claims 29 and 30 are rejected under 35 U.S.C. §102(b) as being anticipated by each of Aaron II and Miller.

Claims 26, 29 and 30 stand rejected under 35 U.S.C. §103(a) as being unpatentable over each Hallas, Aaron, Aaron II, Barker or Mueller.

Claims 20-25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over each Hallas, Aaron, Aaron II, Barker or Mueller taken in combination with each of U.S. Patent No. 5,561,045 ("Dorval") or U.S. Patent No. 6,183,968 ("Bandman").

REJECTION OF CLAIMS 20-37 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Applicant has amended claims 20-26, 29, 31, 38 and 43 to address the issues raised by the Examiner. These issues are discussed in the order in which they were listed in the Official Action.

With respect to claim 38, the Examiner has pointed out in paragraph 4 in the Official Action that the specification is enabling for some of the compounds with end-terminal amino groups of claim 20 but that the process as set forth in claim 38 which refers to claim 20 is not enabling when these amino groups are replaced by the groups $-OR_9$ and/or $=O$. In order to obviate the rejection, applicant has amended claim 38 adding a proviso to eliminate the replacement. Thus, the formula I in claim 38 is limited to the end-terminal amino groups, as compared to example J 42 in the specification where the end-terminal amino groups are replaced. All other compounds where the amino groups are present

can be obtained through the general process as set forth in claim 38. Should the target molecule in R₄ not be hydrogen, then alternative to the direct synthesis as set forth in claim 38, an intermediary product can be obtained also according to the process of claim 38 in which R₄ is hydrogen. This intermediary, according to the examples as set forth in the description, can be further converted into an anthrone after further reacting with a metal-organic compound, and hydrolysis and oxidation, finally converted into the end product. Thus, it should be noted that the compounds JF 22, JF 17, JF 30, JF 32, JF 36 and JF 37 can all be produced according to the process as claimed in claim 38. The examples given are simply alternative possibilities of how they can be represented.

The amendment to claim 38 is supported by the specification and within the scope of the specification.

Concerning paragraph 4a, the compounds of formula I have hydrogen always in para-position. With respect to paragraph 5 of the Official Action, the Examiner's comments with respect to the rejection of claims 20-37 that the specification is enabling for use of the compounds of formula I as labeling agents for immunoassays etc. when the claimed compounds are conjugated to a biomolecules and allegedly not enabling for a method in any other context, is confusing and not readily understood.

Applicant has made every effort to understand the rejections and address all issues. Accordingly, claim 20 was amended to set forth a labeling method for analytes. Applicant respectfully disagrees with the Examiner's postulation that the claimed compounds are enabled as labeling agents for immunoassays and

nucleic acid hybridization assays when conjugated to a biomolecule, but not in any other context. Applicant points to page 4, lines 5-20 and page 5, lines 5-20 in the specification where *inter alia* it is stated that owing to the virtually arbitrary substituent variation, the properties of the individual compounds can be selected as desired and these compounds are suitable for example for use with serum, blood, plasma and similar.

The compounds according to the present invention represent a novel class of fluorescent dyes with intensive fluorescence in the red range of the spectrum. Thus, they readily find applications where such properties are required. The person skilled in the art will thus be apprised about the applications of these dyes.

In view of the foregoing amendments to the claims and the above discussion, it is submitted that the rejection under 35 U.S.C. §112, first paragraph has been overcome. However, since the Examiner's comments did not fully apprise the applicant as to the enabling or non-enabling features, the Examiner found in claims 20 to 37, it could be that the instant rejection can be met with further support from the description, which the applicant will bring forth upon further clarification by the Examiner.

Withdrawal of the rejection of the claims 20-37 under 35 U.S.C. §112, first paragraph is thus respectfully requested.

REJECTION OF CLAIMS 20-43 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

With respect to the Examiner's rejection based on broad and narrow range limitations as in claim 20, applicant has carefully parsed the claim language to remove the narrow ranges and recite the more limited range in dependent claims. Thus, claims 44-48 newly presented, recite the specific compounds.

With respect to the Examiner's comments under paragraph 6b, it is submitted that the substituents are optional and not required and that also only one substituent can be provided. Substituents from $R_9 - R_{12}$ are also only optionally provided.

With respect to paragraph 6c, applicant states that claim 20 was amended to clarify the language and as currently drafted, the claim reciting a ring system and the respective bonds are now clear from the language.

With respect to 6c, applicant wishes to point out that the ring system can be formed from the substituents at positions R_1 to R_7 and thus can represent a normal carbo-or heterocyclic ring system, as for example is seen from compound 30 (JF 24).

Addressing paragraphs 6d-e, applicant has used the phraseologyat least one of..... to replace the improper locution "or/and", in order to include both conjunctive and disjunctive mode. The phraseat least one of A and B... sets forth the possibility of either A and B or A and B. It is applicant's contention for the moment that this is proper phraseology, however, if there is a more suitable

phrase the Examiner is aware of to express this, applicant will make such changes.

With respect to 6d, as stated prior, applicant uses the phraseologyat least one of... A and B to indicate the use of conjunctive and disjunctive such as "and/or".

With respect to 6e, applicant has placed the recited group into a dependent claim, thereby eliminating this issue.

With respect to 6f, the Examiner's objection regarding polyether is not readily understood. The claim recites that the hydrocarbon group can be unsaturated and branched etc. Applicant believes that polyether can fall under such terminology.

With respect to paragraph 6g, applicant has amended claim 20 so that the O-substitution is symmetrical for each of the amino groups. This is also seen as represented in JF 42 on page 15 of the specification.

With respect to paragraph 6h directed to claim 27 and 28, the claim as currently drafted recites that at least one bridge exists between two substituents and that the bridge can be between R_6 and R_{11} ; and/or between R_7 and R_{12} ; and/or R_1 and R_{10} ; and/or R_2 and R_9 . Applicant has made every effort to express the subjunctive/conjunctive relationship as clearly as possible by the use of the phraseat least one of... A and B.... and semicolons. Should the Examiner find that this way of expressing the subjunctive/conjunctive can be improved, applicant will make such changes as the Examiner might suggest.

With respect to 6i, applicant has amended claim 29 to obviate the term "radical". With respect to 6j directed to claim 31, applicant submits that in the compounds IVc, IVd and IVe, the substituent R_{12} is specified forming a bridge with R_6 , as indicated in the presented formulas.

With respect to 6k, applicant submits that the group capable of co-valent coupling can be present at various substituents in the basic cyclic structure. With respect to 6l, "thio" was changed to – thiol–. With respect to 6m, applicant has amended claim 43 to recite that the process is a one-step process without the need for isolation of any intermediate compounds.

With respect to 6n, applicant notes that the phenyl group carries a dimethylaminogroup at position 4; therefore, the designation 4-dimethylaminophenyl is correct.

The Examiner should note that applicant has made every effort to address each and every of the numerous formal objections and rejections listed in the Official Action and to place the claims into condition where they can be deemed allowable. It is believed that the rejections and objections to the claims have been obviated by the amendments to the claims and the foregoing discussion.

Withdrawal of the rejection of the claims 20-43 under 35 U.S.C. §112, second paragraph is thus respectfully requested.

**REJECTION OF CLAIMS 20-25 UNDER 35 U.S.C. §112, SECOND
PARAGRAPH**

Applicant has amended claim 20-25 so the claims now read on a method of detecting analytes using labeling groups, and setting forth the method steps. As such the claim is a proper method claim. The Examiner is also directed to the companion application Serial No. 09/980,538 in which much of the same issues were addressed and solved and which application was already allowed.

Withdrawal of the rejection of the claim 20-25 under 35 U.S.C. §112, second paragraph is thus respectfully requested.

REJECTION OF CLAIMS 20-25 UNDER 35 U.S.C. §101

The Examiners rejection is noted, but deemed moot in view of the amendments to the claims. Since claims 20 to 25 are no longer claims directed to only "use of", the rejection as to subject matter has been obviated.

Withdrawal of the rejection of the claims 20-25 under 35 U.S.C. §101 is thus respectfully requested.

OBJECTION TO CLAIM 37

In view of the foregoing paragraph with discussion directed to the amendment to claims 20-25 into method claims, applicant submits that claim 37 as now on file is proper, and the objection by the Examiner moot.

REJECTION OF CLAIM 26 UNDER 35 U.S.C. §102(b) AS BEING ANTICIPATED BY EACH OF HALLAS, AARON, AARON II, BARKER OR MUELLER

The rejection under 35 U.S.C. 102(b) is respectfully traversed.

In order to clearly distinguish the present invention from the cited references, applicant has amended claim 26 and incorporated the limitation of claim 27. As a result, the compounds as now claimed possess a basic structure of three rings in addition to at least one more ring and comprising one of the amino groups

None of the references disclose a compound with the bridged groups to form a ring system as claimed.

Consequently, the references do not anticipate the amended claim 26.

Withdrawal of the rejection of claim 26 under 35 U.S.C. §102(b) is thus respectfully requested.

**REJECTION OF CLAIM 29 AND 30 UNDER 35 U.S.C. §102(b) AS BEING
ANTICIPATED BY EACH OF AARON II AND MUELLER**

The rejection under 35 U.S.C. 102(b) is not readily understood since it is substantially identical to the rejection as set forth under paragraph 12c and 12e on page 6 of the Official Action.

In order to clearly distinguish the present invention from the cited references, applicant has amended claim 26 and incorporated the limitation of claim 27. Since claims 29 and 30 depend from claim 26 and therefore contains all the limitations of amended claim 26, these claims are distinguishable over the prior art in the same manner as claim 26. The compounds as now claimed possess a basic structure of three rings in addition to at least one more ring and comprising one of the amino groups

None of the references disclose a compound with the bridged groups to form a ring system as claimed.

Consequently, the references do not anticipate the amended claim 26.

Withdrawal of the rejection of claim 26 under 35 U.S.C. §102(b) is thus respectfully requested.

**REJECTION OF CLAIMS 26, 29 AND 30 UNDER 35 U.S.C. §103(a) AS BEING
UNPATENTABLE OVER EACH OF HALLAS, AARON, AARON II, BARKER
OR MUELLER**

The Examiner has now rejected the original claims as unpatentable over each of the cited references.

In view of the current amendments to claim 26, applicant believes that the each of the cited references has been overcome. While the compounds as taught in the cited references may have various utility as dyes, the compounds as claimed here are not taught by either one of the references. There is nothing in Hallas, Aaron, Aaron II, Braker or Mueller that point to the properties of the compounds in claim 26. Specifically, none of the references teaches that the amino groups are part of a ring system. The incorporation of the amino groups into a ring represents an essential difference in structure which cannot be gleaned from the cited references. Contrary to the Examiner's assumption that related structures would have the same properties, the compounds as presently claimed are structurally different and exhibit a quantitative high yield of fluorescence not found heretofore, so that the claimed structures are not rendered obvious by the cited references.

As for the rejection of the retained dependent claims 29 and 30, these claims depend on claim 26, share its presumably allowable features, and therefore it is respectfully submitted that these claims should also be allowed.

Withdrawal of the rejection of claims 26, 29 and 30 under 35 U.S.C. §103(a) and allowance thereof are thus respectfully requested.

REJECTION OF CLAIMS 20 TO 25 UNDER 35 U.S.C. §103(a) AS BEING UNPATENTABLE OVER EACH OF HALLAS, AARON, AARON II, BARKER OR MUELLER TAKEN IN COMBINATION WITH EACH OF DORVAL OR BANDMAN

The Examiner's rejection is respectfully traversed.

Applicant claims novel carbopyronine fluorescent dyes. However neither the references Hallas, Aaron, Aaron II, Barker or Mueller in combination with Dorval or Bandman teach the claimed carbopyronine dyes. The Hallas, Aaron, Aaron II, Barker or Mueller references have been amply discussed above. A combination of each of these references in combination with either Dorval or Bandman are likewise not rendering the claims obvious.

Dorval describes certain immunoassays by using dyes or inorganic pigments. In column 7, numerous dyes are named in a long list which encompasses virtually all dyes known in the area of dye chemistry. However carbopyronines dyes are not listed. Does the Examiner assume that the *triarylmethane* dyes listed in line 22 include the currently claimed dyes? However, the dyes as claimed here are not part of the triarylmethane dyes. Dorval also does not teach that these dyes could be used in the labeling of analytes. Therefore, the Dorval reference does not teach in the direction of the

claimed compounds or the process of labeling analytes. So any combination with Hallas, Aaron, Aaron II, Barker or Mueller will not bring about the dyes as claimed.

Likewise, the Bandman reference does not add anything further to the already cited references. Bandman describes a general list of classes of dyes in col. 9. However, it is quite evident that no carbopyronine dyes are listed. In view of the multitude of methods in which dyes are utilized for conjugates of dye-nucleic acid, highly specific ones as claimed here are synthesized for very specific properties and must fulfill specific values for size of molecules, potential for electron acceptance, fluorescence decay time and similar. The dyes as claimed are suitable, in particular for labeling, since they show an absorption maximum in a wavelength range with which more cost-effective labeling techniques can be realized. Also they are useful for small dimensioned light sources such as for example He-Ne-lasers, and laser diodes can also be used. As shown in Table 1 in the description, fluorescence maximum for the claimed dyes are in the range of 630 and 680 nm.

In view of the foregoing discussion, it is applicant's contention that none of the references either alone or in combination teach the use of carbopyronine dyes in connection with coupling to biological material.

Withdrawal of the rejection of claims 26, 29 and 30 under 35 U.S.C. §103(a) and allowance thereof are thus respectfully requested.

CONCLUSION

Applicant believes that when the Examiner reconsiders the claims in the light of the above comments, she will agree that the invention is in no way properly met or anticipated or even suggested by any of the references however they are considered.

None of the references discloses a method or compounds for labeling using the carbopyronine dyes as claimed.

In view of the above presented remarks and amendments, it is respectfully submitted that all claims on file should be considered patentably differentiated over the art and should be allowed.

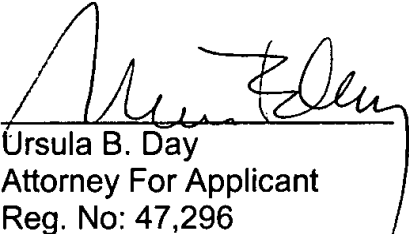
Reconsideration and allowance of the present application are respectfully requested.

Should the Examiner consider necessary or desirable any formal changes anywhere in the specification, claims and/or drawing, then it is respectfully requested that such changes be made by Examiner's Amendment, if the Examiner feels this would facilitate passage of the case to issuance. If the Examiner feels that it might be helpful in advancing this case by calling the undersigned, applicant would greatly appreciate such a telephone interview.

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The Commissioner is hereby authorized to charge fees which may be required, or credit any overpayment to Deposit Account No. 06-0502.

Respectfully submitted,

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